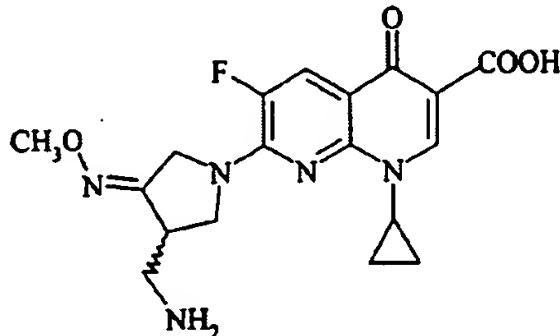


PTO/PCT Rec'd 15 MAR 2001

PROCESS FOR THE PRODUCTION OF A NAPHTHYRIDINE CARBOXYLIC ACID DERIVATIVE
(METHANESULFONATE SESQUIHYDRATE)invent
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The present invention relates to a process for the production of a naphthyridine carboxylic acid derivative having antibacterial activity.

EP 688772 discloses novel naphthyridine carboxylic acid derivatives, including anhydrous (R,S)-7-(3-aminomethyl-4-methoxyiminopyrrolidin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid of formula I, having antibacterial activity.



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WO 98/42705 (published after the priority date of the present application) discloses (R,S)-7-(3-aminomethyl-4-syn-methoxyiminopyrrolidin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid methanesulfonate and hydrates thereof including the sesquihydrate (the "methanesulfonate sesquihydrate").

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WO 98/42705 discloses a process for the production of the methanesulfonate sesquihydrate comprising reaction of the corresponding free base with methanesulfonic acid in dichloromethane / ethanol followed by recrystallisation of the resulting crude salt anhydrate from either water : acetone (10:7 v/v), or water : ethanol (1:2 v/v). The overall yield for this two step process is 70-80%. An alternative process for the production of the methanesulfonate sesquihydrate described in WO 98/42705 comprises exposing a solvate of the methanesulfonate (ethanol 0.11%) to high relative humidity (nitrogen >93% humidity).

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The present invention relates to an improved process for the production of the methanesulfonate sesquihydrate which comprises direct salt and hydrate formation.

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According to the invention there is provided a process for the production of 7-(3-aminomethyl-4-syn-methoxyiminopyrrolidin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid methanesulfonate sesquihydrate which comprises reacting 7-(3-aminomethyl-4-syn-methoxyiminopyrrolidin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid and methanesulfonic acid in a solvent comprising at least one water miscible cosolvent and water, and isolating the resulting solid product.

This is a 371 of international application PCT/EP99/07003, filed September 15, 1999 which claims benefit of GB 9820405.0 filed September 18, 1998.